

SUBMISSION and AMENDMENT UNDER 37 C.F.R. §§1.114 and 1.121

Atty. Dkt. No. 0618.017.0002

Serial No.: 10/091,430

Filing Date: March 7, 2002

**REMARKS**

Claims 73, 74, 78, 79 and 81 have been amended and claim 93 has been added. Claims 83-92 have been canceled. The claims have been amended or canceled to expedite prosecution and to more clearly define envisioned commercial embodiments. In particular, the amendments to independent claim 73 clarify that the buffer used in the ion buffer reservoir of the apparatus inhibits the migration of ions into the gel body, and that this buffer comprises a Zwitter ion and an amine. Similarly, claim 81 has been amended to indicate that the migration of ions originates from the electrochemically ionizable metal.

Support for the amendments to the claims and the newly added claim is found throughout the specification and the originally presented claims and thus do not add new matter. For example the inhibition of ion migration into the gel during electrophoresis by buffers that comprise a zwitter ion and an amine is supported in the specification, including the Examples. In referring to an electrophoresis apparatus of the invention, the specification states on page 3, lines 19-21 and lines 28-30: " The anode is made of an electrochemically ionizable metal, and the electrolyte solution is of a composition such that migration of ions generated by the anode is inhibited." In a later passage, page 9, lines 7-13, the specification states:

An unexpected result of using some of the embodiments of the electrolyte solutions of the present invention in combination with ionizable metal, is that the migration of metal ions through the gel is inhibited, . . . When amine molecules and "Zwitter ions" (ZI) are used the ZI acts as the main buffering agent at zone A adjacent to cathode 21. However, the amine molecules play a role as well.

The application then provides several Examples of buffers that comprise an amine and a Zwitter ion, in which the buffer inhibits migration of metal ions of the anode into the body of separating gel during electrophoresis, as stated in amended claim 73 (Examples 1, 2, 3, 6, and 7).

Accordingly, no new matter has been introduced by way of these claim amendments, and claims 73-76, 78-82 and 93 are now pending in the application.

SUBMISSION and AMENDMENT UNDER 37 C.F.R. §§1.114 and 1.121

Atty. Dkt. No. 0618.017.0002

Serial No.: 10/091,430

Filing Date: March 7, 2002

Office Action of January 25, 2005**35 U.S.C. § 102 Rejections**

The Office Action mailed January 25, 2005, rejects claims 73-76, 80, 82-86, 90, and 92 under 35 U.S.C. § 102(b), as being anticipated by Cabilly et al. (WO 97/41070). In view of the foregoing claim amendments, which were made to expedite prosecution, the Examiner's rejection of claims 73-76, 80, 82-86, 90 and 92 under 35 U.S.C. §102(b) is now moot.

Applicants have amended independent claim 73 to more clearly define commercial embodiments. As amended, independent claim 73 incorporates elements of canceled claim 77, which recited an anode buffer reservoir where the buffer comprises an amine and a zwitter ion.

In contrast to the present application, Cabilly et al. does not disclose an electrophoresis apparatus that includes an anode comprising an electrochemically ionizable metal, in which the anode is located in a semi-solid ion reservoir containing a buffer having an amine component and a Zwitter ion, in which the buffer inhibits the migration of metal ions into the gel during electrophoresis, as set forth in independent claim 73 as amended.

Cabilly et al. discloses the use of a Tris-acetate EDTA (TAE) anode buffer. Neither tris-acetate nor EDTA are Zwitter ions. Thus, Cabilly et al. does not disclose a buffer having an amine component and a Zwitter ion in the anode buffer reservoir.

In the present invention, a buffer that includes an amine and a Zwitter ion, as set forth in claim 73, inhibits the migration of interfering ions that originate from the ionizable metal and prevents them from penetrating into the running zone (the body of the electrophoresis gel), thereby eliminating the need for an ion exchange matrix. Since Cabilly et al. does not disclose a buffer having an amine component and a Zwitter ion in the anode buffer reservoir, Cabilly et al. does not disclose each and every element of independent claim 73 as amended. Therefore, Cabilly et al. does not anticipate newly amended claim 73, and its dependent claims under 35 U.S.C. § 102(b). Reconsideration and withdrawal of this rejection is earnestly solicited.

SUBMISSION and AMENDMENT UNDER 37 C.F.R. §§1.114 and 1.121

Atty. Dkt. No. 0618.017.0002

Serial No.: 10/091,430

Filing Date: March 7, 2002

**35 U.S.C. § 103 Rejections****Claims 77-79 and 87-89**

Claims 77, 78, 79, 87, 88, and 89 were rejected under 35 U.S.C. § 103(a) as being obvious over Cabilly et al. in view of Monthony et al (U.S.P.N. 3,948,743). In view of the amendments to the claims and the cancellation of claims 77 and 87, 88 and 89 the rejection under 35U.S.C. §103(a) is now moot.

The requirements for establishing a *prima facie* case of obviousness under 35 U.S.C. § 103(a) include: 1) each and every element of the claimed invention must be taught or suggested by the cited references (MPEP 2142); 2) there must be a suggestion or motivation to combine the cited references, and 3) that one of ordinary skill in the art would have a reasonable expectation of success in combining or modifying the teachings of the cited references to arrive at the claimed invention. Furthermore, even where a *prima facie* case can be established, an obviousness rejection can be overcome by a showing of secondary factors such as a long-felt need, commercial success, or unexpected results (MPEP 2141).

Applicants assert that the cited references, alone or in combination, do not render the present invention obvious because there is no suggestion or motivation to combine the references with a reasonable expectation of success. Furthermore, the unexpected results provided by the invention further establish that the present invention is not rendered obvious by the cited references.

With regard to the lack of suggestion or motivation to combine references, it is noted that the disclosure in Cabilly et al., which discloses the use of copper, lead, or silver anodes, does not teach the selection of an anode of an "electrochemically ionizable metal" for use with buffers having a zwitter ion component and an amine component, as recited in amended claim 73. There is also no teaching in Monthony et al., which discloses the use of a Tris-glycine buffer, of any advantages of electrophoresis buffers containing a zwitter ion and an amine in combination with particular anode compositions. Thus the references, alone or in combination, do not provide any

SUBMISSION and AMENDMENT UNDER 37 C.F.R. §§1.114 and 1.121

Atty. Dkt. No. 0618.017.0002

Serial No.: 10/091,430

Filing Date: March 7, 2002

suggestion for one skilled in the art to combine an electrochemically ionizable metal anode with a zwitterion/amine buffer in the anode buffer reservoir in an electrophoresis system.

At the time the invention was made, there was no suggestion or motivation for combining the teachings of the cited references. Prior to the invention, the following issues that arise in the electrophoresis of biomolecules were recognized: (1) the generation of protons and hydroxyl ions at the electrodes during electrophoresis alters the pH of the running buffer, leading to nonoptimal results; (2) the use of an ionizable metal electrode prevents the formation of protons at the anode, and instead causes the formation and release of metal ions into the running buffer; and (3) the migration of metal ions into the gel interferes with electrophoresis. The invention, however, relies on the inventors obtaining the surprising result that the migration of metal ions into the gel during electrophoresis can actually be prevented by use of particular buffers, namely, electrophoresis buffers described in the application that include a zwitter ion and an amine. It would not have been obvious to one of skill in the art, therefore, that a buffer that comprises a combination of a zwitter ion and an amine would solve the above-noted problems associated with electrophoresis at that time of the invention.

Furthermore, at the time the invention was made, there was no motivation found in the art or in the problem itself to use a buffer comprising a zwitter ion and an amine. Indeed, Cabilly et al. addresses the problem of ion interference by combining an electrode of ionizable metal with a zwitter ion/amine buffer and provides an alternate solution by the use of ion exchange matrices in the electrode reservoirs, as disclosed in Cabilly et al. In addition, the use of ionizable metal electrodes would not have been an obvious solution to the problems at hand, since the use of ionizable metal also led to problems of ion generation (which, however, could also be ameliorated by the inclusion of ion exchange matrices). Also, there was no teaching or suggestion in the art that a particular buffer (in the absence of an ion exchange mechanism) could prevent metal ion migration during electrophoresis. Cabilly et al., for example, suggests a different strategy --the use of an ion exchange matrix--to reduce ion migration into the gel.

As another method of eliminating interference by ion migration, Cabilly et al. suggests the use of long gels, such that electrophoretic separation of biomolecules could occur in one area

SUBMISSION and AMENDMENT UNDER 37 C.F.R. §§1.114 and 1.121

Atty. Dkt. No. 0618.017.0002

Serial No.: 10/091,430

Filing Date: March 7, 2002

of the gel, and ion migration into the anode end of the gel would not reach the area of biomolecule separation before separation was complete (page 22, line 34 – page 23, line 8).

In summary, there was no suggestion or motivation before the present application was filed, to use amine and zwitter ion buffers with electrodes that release metal ions into the electrophoresis medium. Without such a motivation to combine references with an expectation of success, the Office Action of January 25, 2005 simply uses hindsight picking and choosing elements from the cited references to arrive at the claimed invention. As is well-established, this hindsight picking and choosing of elements is impermissible in determining the obviousness of the invention. (*See* MPEP 2142)

For the same reasons, one skilled in the art would not have had a reasonable expectation of success in inhibiting ion migration during electrophoresis by using a zwitter ion / amine based buffer. At the time the invention was made, it was not known or expected that particular buffers might inhibit ion migration during electrophoresis. Thus one of ordinary skill in the art would not expect to succeed in inhibiting ion migration into gels using the approach of testing different types of buffers with electrochemically ionizable metal electrodes.

Further, Applicants assert that even if a *prima facie* case of obviousness can be made against the claimed invention, using the cited references, that the unexpected result obtained by the inventors vitiates the obviousness rejection. In the present invention, the novel use of a zwitterion/amine buffer in an electrophoresis apparatus that has an electrochemically ionizable metal anode led to the unexpected result of inhibiting metal ion migration into the gel body that occurs at the anode end of the gel during electrophoresis. As detailed above, in the prior art (e.g., Cabilly et al.) an ion exchange matrix was used to overcome the problem of  $H^+$  or metal ion generation at the anode and its effects during electrophoresis. The present invention eliminates the need for an ion exchange matrix in the buffer reservoir to overcome these effects. Thus, the unexpected results of the present invention further establish that the claimed invention is not rendered obvious by the cited references.

SUBMISSION and AMENDMENT UNDER 37 C.F.R. §§1.114 and 1.121

Atty. Dkt. No. 0618.017.0002

Serial No.: 10/091,430

Filing Date: March 7, 2002

In summary, Applicants assert that the Office Action of January 25, 2005 failed to establish a *prima facie* case of obviousness under 35 U.S.C. §103(a) against the previously pending claims because there is no suggestion or motivation to combine the teachings of the cited references, and because there is no reasonable expectation of success in combining the references to arrive at the claimed invention. The case for obviousness under 35 U.S.C. § 103(a) is further rebutted by the unexpected result obtaining in practicing the invention. Reconsideration and withdrawal of this rejection are earnestly solicited.

#### **Claims 81 and 91**

Claims 81 and 91 were rejected in the Office Action as being obvious over Cabilly et al. Applicants respectfully traverse this rejection. In view of the amendment to the claims and the cancellation of claim 91, the Rejection of claims 81 and 91 is now moot.

Claim 81 as amended is drawn to an apparatus in which the metal ions do not migrate into the separating gel during electrophoresis. Claim 81 depends from claim 73 and thus incorporates all the limitations of claim 73. Independent claim 73 has been amended herein to recite a buffer that comprises a zwitterion and an amine. As discussed above, Cabilly et al. does not disclose or suggest the use of a buffer that comprises a zwitter ion and an amine. Thus, because Cabilly et al. does not contain each and every limitation of the claimed invention, Cabilly et al. does not render obvious the invention of claim 81. Reconsideration and withdrawal of this rejection are earnestly solicited.

SUBMISSION and AMENDMENT UNDER 37 C.F.R. §§1.114 and 1.121

Atty. Dkt. No. 0618.017.0002

Serial No.: 10/091,430

Filing Date: March 7, 2002

CONCLUSION

In view of the foregoing amendments and remarks, the pending claims are deemed to be allowable. Their favorable reconsideration and allowance is respectfully requested.

Should the Examiner believe that further discussion of any remaining issues would advance the prosecution, he or she is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,

Date: October 11, 2005

Castellano Malm Ferrario & Buck PLLC

Customer Number: **43446**

Telephone: (202) 478-5300

Facsimile: (202) 318-1288

By

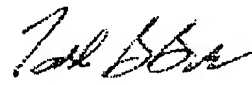


Todd B. Buck  
Registration No. 48,574

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being facsimile transmitted or deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 11<sup>th</sup> day of October, 2005.

Todd B. Buck

Name



Signature